

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Alvaro SANCHEZ-FERRER et al

Serial No.: 10/125554

Group Art Unit: 1651

Filed: April 19, 2002

Examiner: Herbert J. Lilling

For: PROCESS FOR PREPARING
CEPHALOSPORANIC DERIVATIVES

SECOND INFORMATION DISCLOSURE STATEMENT

Commissioner of Patents
Washington, DC 20231

Sir:

As a means of complying with the duty of disclosure under 37 CFR §1.56, and in accordance with 37 CFR §§1.97 and 1.98, Applicant(s), through the undersigned attorney, submits this Information Disclosure Statement. The patents, publications or other information submitted herewith are listed on the attached Form PTO-1449 and copies are attached.

The documents listed on the attached Form PTO-1449 were cited in an Partial International Search Report issued in a corresponding PCT application (PCT/EP02/04354).

Document AC is the English counterpart of German Application DE1953861A.

Document AJ is the English counterpart of Document AK.

Document AE is the English counterpart of Document AL.

Document AA is the English counterpart of Document AS.

Document AB is the English counterpart of Document AU.

Document AF is the English counterpart of Document AN.

Document AD is the English counterpart of Document AZ.

The documents listed in the Partial Search Report but not attached have been previously submitted with the IDS filed June 19, 2002.

In accordance with 37 CFR §1.97(b)(3), this Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits of the above-identified application.

Respectfully submitted,

JACOBSON HOLMAN PLLC

By: _____
John C. Holman
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Date: December 16, 2002

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
JOHN A O'BRIEN & ASSOCIATES
Third Floor
Attn. O'BRIEN, John A.
Duncairn House
14 Carysfort Avenue
Blackrock, County Dublin
IRELAND

INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

Date of mailing (day/month/year) 06/09/2002	
Applicant's or agent's file reference BFM002/C/WO	PAYMENT DUE within 30 xxx days/days from the above date of mailing
International application No. PCT/EP 02/ 04354	International filing date (day/month/year) 18/04/2002
Applicant BIOFERMA MURCIA, S.A.	

1. This International Searching Authority

- (i) considers that there are 4 (number of) inventions claimed in the international application covered by the claims indicated ~~xxx~~ on the extra sheet:

and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated ~~xxx~~ on the extra sheet:

- (ii) ☒ has carried out a partial international search (see Annex) ☐ will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:

1-19, 23-38, 39-41

- (iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid


2. The applicant is hereby **invited**, within the time limit indicated above, to pay the amount indicated below:

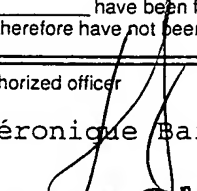
EUR 945, - x 3 = EUR 2 835, -
 Fee per additional invention number of additional inventions total amount of additional fees

Or, _____ x _____ = _____

The applicant is informed that, according to Rule 40.2(c), the payment of any additional fee may be made under protest, i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. ☐ Claim(s) Nos. _____ have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority

 European Patent Office, P.B. 5818 Patentlaan 2
 NL-2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

 Véronique Baillou

EINSCHREIBEN

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-19,23-38,39-41

Enzymatic process for the production of 3-thiolated 7-aminocephalosporanic acid derivatives, compounds of formula I used in that process and a process for the production thereof

2. Claim : 20

3-Thiolated-7-ACA of formula III

3. Claims: 21-22

Process for the production of Cephalosporin C antibiotics via enzymation of compounds of formula III

4. Claims: 42-43

Process for the production of Cephalosporin C antibiotics via enzymation of compounds of formula I

Prior art as represented by the documents cited in the Search Report and cited by the Applicant discloses various processes for the enzymatic conversion of cephalosporin C compounds into the corresponding alpha-ketoglutaric derivatives and further into 7-ACA derivatives. Given this state of the art the technical problem was to provide other enzymatic processes for the production of these compounds. The solution of the problem is alleged to be the provision of a process as claimed in Claims 1-19, compounds of formula I used as starting materials in this process as claimed in Claims 39 to 41 and a process for their production as claimed in Claims 23-38.

Claim 20 is claiming 3-thiolated-7-ACA derivatives of formula III prepared by the process of Claim 1. Such derivatives are already known in the state of the art.

Claims 21 and 22 disclose a process for the production of Cephalosporin C antibiotics via enzymation of compounds of formula III.

Claims 42 and 43 refer to processes for the production of Cephalosporin C antibiotics via enzymation of compounds of formula I.

Since the provision of the end product of the claimed process and such processes directed to the production of compounds different in structure is totally unrelated to the problem of providing another process for the production of cephalosporin C compounds it is considered that the processes claimed in Claims 1-19 and 23-38 and the processes claimed in Claims 21/22 and 42/43 and the products claimed in Claim 20, respectively, are not linked by a single inventive concept, and that the application therefore lacks unity of invention (Article 82 EPC).

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:
2. see 'Invitation to pay additional fees'
This communication is not the international search report which will be established according to Article 18 and Rule 43.
3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.
4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JUSTIZ OH ET AL: "One-pot chemoenzymatic synthesis of 3'-functionalized cephalosporines (cefazolin) by three consecutive biotransformations in fully aqueous medium" JOURNAL OF ORGANIC CHEMISTRY, vol. 62, no. 26, 1997, pages 9099-9106, XP002177920 cited in the application schemes 4, 5 page 9103, right-hand column, last paragraph -page 9104, left-hand column, paragraph 2 page 9105, right-hand column, last paragraph ---	1-23
X	"The Merck Index on CD-ROM, Version 12:2" 1997, MERCK & CO INC., WHITEHOUSE STATION, NJ, USA XP002177921 Cefazolin (Entry 1967), Ceftriaxone (entry 2001), Cefotiam (entry 1985), Cefatrizine (entry 1965), Cefamandole (entry 1964), Cefoperazone (entry 1981), Cefazedone (entry 1966) ---	20
Y	WO 90 12110 A (BIOPURE CORP) 18 October 1990 (1990-10-18) page 3, line 13 - line 16; claim 1 claims 1,10 --- -/--	1-19

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Annex to Form PCT/ISA/206
**COMMUNICATION RELATING TO THE RESULTS
 OF THE PARTIAL INTERNATIONAL SEARCH**

International Application No
PC1/EP 02/04354

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 20 56 983 A (CIBA-GEIGY AG) 9 June 1971 (1971-06-09) example 2 ---	39,40
Y	DE 19 53 861 A (FUJISAWA PHARMACEUTICAL CO., LTD.) 6 May 1971 (1971-05-06) claims 1-21 ---	1-23
Y	EP 0 436 355 A (FUJISAWA PHARMACEUTICAL CO.) 10 July 1991 (1991-07-10) claim 1 ---	1-23
Y	EP 0 583 817 A (ASAHI KASEI KOGYO KABUSHIKI KAISHA) 23 February 1994 (1994-02-23) claims 1-12 ---	1-38
Y	EP 0 492 495 A (HOECHST AG) 1 July 1992 (1992-07-01) claims 1-6 ---	1-38
Y	EP 0 517 200 A (MINISTERO DELL'UNIVERSITA' E DELLA RICERCA SCIENTIFICA E TECNOLOGICA) 9 December 1992 (1992-12-09) cited in the application claims 1-10 ---	1-38
Y	WO 00 78989 A (ANTIBIOTICOS, S.A.U.) 28 December 2000 (2000-12-28) claims 1-37 ---	1-23
X	DE 19 39 341 A (GLAXO LABORATORIES LTD.) 5 February 1970 (1970-02-05) claims 1-40; example 13 ---	1-23
Y	PATENT ABSTRACTS OF JAPAN vol. 005, no. 152, 25 September 1981 (1981-09-25) & JP 56 085298 A (ASAHI CHEM. IND. CO.) abstract ---	1-38
Y	PATENT ABSTRACTS OF JAPAN vol. 011, no. 322, 20 October 1987 (1987-10-20) & JP 62 107798 A (ASAHI CHEM. IND. CO.), 19 May 1987 (1987-05-19) abstract ---	1-38
Y	GB 1 385 685 A (GLAXO LABORATORIES LTD.) 26 February 1975 (1975-02-26) claims 1-40 ---	1-38
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	J. E. BALDWIN ET AL.: "Cleavage of the 5-amino-5-carboxy-2-oxapentanoyl side chain from enzymatically synthesised penicillins and cephalosporins" BIOORG. MED. CHEM. LETT., vol. 5, no. 21, 1995, pages 2507-2512, XP002207185 cited in the application * Schemes 2 and 4 *	1-19
Y	EP 0 496 993 A (ANTIBIOTICOS SPA) 5 August 1992 (1992-08-05) claims 1-12	1-23
Y	CH 520 709 A (GLAXO LABORATORIES LTD.) 31 March 1972 (1972-03-31) claim 1	23
Y	CONLON HUGH D ET AL.: "Two-step immobilized enzyme conversion of cephalosporin C to 7-aminocephalosporanic acid" BIOTECHNOLOGY AND BIOENGINEERING, vol. 46, no. 6, 1995, pages 510-513, XP001093638 tables I-IV	1-38
X	DATABASE CROSSFIRE BEILSTEIN [Online] Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. 1198450/ XP002211689 abstract & DE 21 37 386 A (TAKEDA CHEM. IND.) 31 May 1972 (1972-05-31)	39
X	DATABASE CROSSFIRE BEILSTEIN [Online] Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. 599207 XP002211690 abstract & CH 601 312 A (FUJISAWA PHARM.) 14 July 1978 (1978-07-14)	39,40

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Annex to Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS
OF THE PARTIAL INTERNATIONAL SEARCH

International Application No
PC1/EP 02/04354

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE CROSSFIRE BEILSTEIN [Online] Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. 600138 XP002211691 abstract & DE 22 39 947 A (TAKEDA CHEM. IND.) 15 March 1973 (1973-03-15)</p>	39
X	<p>DATABASE CROSSFIRE BEILSTEIN [Online] Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. 1097400,1062954,1061615 XP002211692 abstract & ZA 6 802 695 A (FUJISAWA PHARM. CO.) 1967</p>	39,40
X	<p>--- CHEMICAL ABSTRACTS, vol. 80, no. 13, 1 April 1974 (1974-04-01) Columbus, Ohio, US; abstract no. 70820t, page 348; XP002207187 abstract & JP 48 075587 A (FUJISAWA PHARMACEUTICAL CO., LTD.) 11 October 1973 (1973-10-11)</p>	39,40
Y	<p>--- CHEMICAL ABSTRACTS, vol. 86, no. 15, 11 April 1977 (1977-04-11) Columbus, Ohio, US; abstract no. 106611r, page 514; XP002207186 abstract & JP 51 088694 A (TOYO JOZO CO., LTD.) 3 August 1976 (1976-08-03)</p>	1-38
X	<p>--- DE 23 32 045 A (FUJISAWA PHARMACEUTICAL CO. LTD.) 10 January 1974 (1974-01-10) claims 16,19</p>	39
X	<p>--- DE 26 26 026 A (MERCK PATENT GMBH) 22 December 1977 (1977-12-22) claim 1</p> <p>--- -/--</p>	39,40